Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (Withdrawn-Previously presented). A method of preparing a heteromultimer comprising a first polypeptide and a second polypeptide which meet at an engineered interface, wherein said engineered interface further comprises an interface of the first polypeptide and an interface of the second polypeptide and wherein either: (i) the interface of the first polypeptide comprises a protuberance which is positionable in a cavity in the interface of the second polypeptide, and/or (ii) the interface of the first polypeptide comprises a cavity which is positionable in a protuberance of the second polypeptide; the method comprising the steps of:

(a) culturing a host cell comprising nucleic acid encoding the first polypeptide and second polypeptide, wherein the nucleic acid encoding the first polypeptide has been altered from the original nucleic acid to encode the protuberance or the nucleic acid encoding the second polypeptide has been altered from the original nucleic acid to encode the cavity, or both, and wherein the culturing is such that the nucleic acid is expressed; and

(b) recovering the heteromultimer from the host cell culture

wherein the ratio of heteromultimer:homomultimer that forms is greater than for multimer having a non-engineered interface.

2 (Withdrawn). The method of claim 1 wherein the nucleic acid encoding the first polypeptide has been altered from the original nucleic acid to encode the protuberance and the nucleic acid encoding the second polypeptide has been altered from the original nucleic acid to encode the cavity.

3 (Withdrawn). The method of claim 1 wherein step (a) is preceded by a step wherein nucleic acid encoding an original residue from the interface of the first polypeptide is replaced with nucleic acid encoding an import residue having a larger side chain volume than the original residue.

4 (Withdrawn). The method of claim 3 wherein the import residue is arginine (R).

5 (Withdrawn). The method of claim 3 wherein the import residue is phenylalanine (F).

6 (Withdrawn). The method of claim 3 wherein the import residue is tyrosine (Y).

7 (Withdrawn). The method of claim 3 wherein the import residue is tryptophan (W).

8 (Withdrawn). The method of claim 1 wherein step (a) is preceded by a step wherein nucleic acid encoding an original residue in the interface of the second polypeptide is replaced with nucleic acid encoding an import residue having a smaller side chain volume than the original residue.

9 (Withdrawn). The method of claim 8 wherein the import residue is not cysteine (C).

10 (Withdrawn). The method of claim 8 wherein the import residue is alanine (A).

11 (Withdrawn). The method of claim 8 wherein the import residue is serine (S).

12 (Withdrawn). The method of claim 8 wherein the import residue is threonine (T).

13 (Withdrawn). The method of claim 8 wherein the import residue is valine (V).

14 (Withdrawn). The method of claim 1 wherein the first and second polypeptide each

comprise an antibody constant domain.

15 (Withdrawn). The method of claim 14 wherein the antibody constant domain is a C_H3 domain.

16 (Withdrawn). The method of claim 15 wherein the antibody constant domain is from an IgG.

17 (Withdrawn). The method of claim 16 wherein the IgG is human IgG_1.

18 (Withdrawn). The method of claim 1 wherein the heteromultimer is a bispecific antibody.

19 (Withdrawn). The method of claim 1 wherein the heteromultimer is a bispecific immunoadhesin.

20 (Withdrawn). The method of claim 1 wherein the heteromultimer is an antibody-immunoadhesin chimera.

21 (Withdrawn). The method of claim 3 wherein one original residue from the first polypeptide has been replaced with an import residue.

22 (Withdrawn). The method of claim 8 wherein one original residue from the second polypeptide has been replaced with an import residue.

23 (Withdrawn). The method of claim 1 wherein step (a) is preceded by a step wherein the

nucleic acid encoding the first and second polypeptide is introduced into the host cell.

24 (Cancelled)

25 (Previously presented). An isolated heteromultimer comprising a first polypeptide and a second polypeptide which meet at an engineered interface, wherein said engineered interface further comprises an interface of the first polypeptide and an interface of the second polypeptide:

(a) the interface of the first polypeptide comprises a protuberance that is positionable in a cavity in the interface of the second polypeptide, or

(b) the interface of the first polypeptide comprises a cavity that is positionable in a protuberance of the second polypeptide,

wherein the protuberance or cavity, or both, have been introduced into the engineered interface such that a greater ratio of heteromultimer:homomultimer forms than for a multimer having a non-engineered interface.

26 - 27 (Cancelled).

28 (Previously presented). A composition comprising the heteromultimer of any of claims 25, 39, 57-59, 66, 75, and 81 and a pharmaceutically acceptable carrier.

29 (Withdrawn). A host cell comprising nucleic acid encoding the heteromultimer of claim 25.

30 (Withdrawn). The host cell of claim 29 wherein the nucleic acid encoding the first polypeptide and the nucleic acid encoding the second polypeptide are present in a single vector.

31 (Withdrawn). The host cell of claim 29 wherein the nucleic acid encoding the first polypeptide and the nucleic acid encoding the second polypeptide are present in separate vectors.

32 (Withdrawn). A method of making a heteromultimer comprising culturing the host cell of claim 29 so that the nucleic acid is expressed and recovering the heteromultimer from the cell culture.

33 (Withdrawn). The method of claim 32 wherein the host cell is a mammalian cell.

34 (Withdrawn). The method of claim 32 wherein the heteromultimer is recovered from the cell culture media.

35 (Withdrawn-Previously presented). A method of preparing a heteromultimer comprising a first and second polypeptide that meet at an engineered interface, wherein said engineered interface further comprises an interface of the first polypeptide and an interface of the second polypeptide comprising:

(a) altering a first nucleic acid encoding the first polypeptide so that an amino acid residue in the interface of the first polypeptide is replaced with an amino acid residue having a larger side chain volume, thereby generating a protuberance on the first polypeptide;

(b) altering a second nucleic acid encoding the second polypeptide so that an amino acid residue in the interface of the second polypeptide is replaced with an amino acid residue having a smaller side chain volume, thereby generating a cavity in the second polypeptide, wherein the protuberance is positionable in the cavity;

(c) introducing into a host cell the first and second nucleic acids and culturing the cell so that expression of the first and second nucleic acid occurs;

(d) recovering the heteromultimer formed from the cell culture

wherein a greater ratio of heteromultimer:homomultimer forms than for a multimer having a non-engineered interface.

36 (Withdrawn). The method of claim 35 wherein the first and second polypeptide each

comprise an antibody constant domain.

37 (Withdrawn). The method of claim 35 wherein the antibody constant domain is a C_H3 domain.

38 (Withdrawn). The method of claim 37 wherein the antibody constant domain is from a human IgG.

39 (Previously presented). The heteromultimer of Claim 25 wherein the interface comprises both (a) and (b).

40 - 41 (Canceled).

42 (Previously presented). The heteromultimer of Claim 25 wherein the protuberance has been introduced into the engineered interface.

43 (Previously presented). The heteromultimer of Claim 25 wherein the cavity has been introduced into the engineered interface.

44 (Previously presented). The heteromultimer of Claim 42, wherein protuberance comprises a non-naturally occurring amino acid residue.

45 (Previously presented) The heteromultimer of Claim 42, wherein the protuberance comprises a naturally occurring amino acid residue.

46 (Previously presented). The heteromultimer of Claim 45, wherein the protuberance comprises an arginine (R) residue.

47 (Previously presented). The heteromultimer of Claim 45, wherein the protuberance comprises a phenylalanine (F) residue.

48 (Previously presented). The heteromultimer of Claim 45, wherein the protuberance comprises a tyrosine (Y) residue.

49 (Previously presented). The heteromultimer of Claim 45, wherein the protuberance comprises a tryptophan (W) residue.

50 (Previously presented). The heteromultimer of Claim 42, wherein the cavity comprises a non-naturally occurring amino acid residue.

51 (Previously presented). The heteromultimer of Claim 42, wherein the cavity comprises a naturally occurring amino acid residue.

52 (Previously presented). The heteromultimer of Claim 51, wherein the cavity comprises an alanine (A) residue.

53 (Previously presented). The heteromultimer of Claim 51, wherein the cavity comprises a serine (S) residue.

54 (Previously presented). The heteromultimer of Claim 51, wherein the cavity comprises a threonine (T) residue.

55 (Previously presented). The heteromultimer of Claim 51, wherein the cavity comprises a valine (V) residue.

56 (Cancelled).

57 (Previously presented). The heteromultimer of Claim 25, wherein the engineered interface comprises an immunoglobulin constant domain.

58 (Previously presented). The heteromultimer of Claim 57, wherein the immunoglobulin constant domain is a C_H3 domain.

59 (Previously presented). The heteromultimer of Claim 58, wherein the C_H3 domain is from an IgG.

60 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG1 subtype.

61 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG2 subtype.

62 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG2A subtype.

63 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG2B subtype.

64 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG3 subtype.

65 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG4 subtype.

66 (Previously presented). The heteromultimer of Claim 25, wherein the first or second polypeptide further comprises a binding domain.

67 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is an antigen binding domain.

68 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is a ligand binding domain.

69 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is a receptor binding domain.

70 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is an enzymatic domain.

71 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is an antibody variable domain.

72 (Previously presented). The heteromultimer of Claim 25 which is a multi-specific antibody.

73 (Previously presented). The heteromultimer of Claim 72 which is a bi-specific antibody.

74 (Previously presented). The heteromultimer of Claim 72 which is a tri-specific antibody.

75 (Previously presented). The heteromultimer of Claim 25 which is an immunoadhesin.

76 (Previously presented). The heteromultimer of Claim 75 which is a multi-specific immunoadhesin.

77 (Previously presented). The heteromultimer of Claim 76 which is a bi-specific immunoadhesin.

78 (Previously presented). The heteromultimer of Claim 76 which is a heterodimer.

79 (Previously presented). The heteromultimer of Claim 76 which is a heterotrimer.

80 (Previously presented). The heteromultimer of Claim 76 which is a heterotetramer.

81 (Previously presented). The heteromultimer of Claim 25 which is an antibody-immunoadhesin chimera.